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OPTIMIZING SURFACTANT CONCENTRATION FOR CONTROLLING PLGA NANOPARTICLE SIZE IN DRUG DELIVERY APPLICATIONS

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ABSTRACT

Nanoparticles have emerged as versatile drug delivery vehicles suitable for a wide range of administration routes. Over time, researchers have explored numerous natural and synthetic polymers for nanoparticle preparation, with particular focus on Poly(lactic acid) (PLA), Poly(glycolic acid) (PGA), and their copolymers (PLGA) due to their favorable biocompatibility and biodegradability. These nanoparticles serve as carriers for various drug classes, including anticancer agents, antihypertensive drugs, immunomodulators, and hormones, as well as macromolecules like nucleic acids, proteins, peptides, and antibodies. This study investigates the impact of surfactant concentration on the size of poly(lactic-co-glycolic acid) (PLGA) nanoparticles. Through a systematic exploration of different surfactant concentrations, ranging from low to high levels, the size distribution of PLGA nanoparticles is analyzed using dynamic light scattering (DLS) or similar techniques. The abstract summarizes the observed relationship between surfactant concentration and nanoparticle size, providing insights into the optimal conditions for controlling PLGA nanoparticle size in various applications, from drug delivery to biomedical engineering.

Keywords: PLGA (poly lactide co-glycolide), Pluronic F68, surfactant, Dynamic Light Scattering

1. INTRODUCTION

Nanotechnology is widely employed in many fields, including forensic science, electronics, fiber and textiles (Perelshtein *et al.,* 2008), agriculture (B. Speiser *et al.,* 2008; Lai *et al.,* 2006), forensic science (Choi *et al.,* 2008), medical therapeutics,

and electronics (Huang *et al.,* 2003). Owing to their capacity to transport a wide variety of medications to different parts of the body for extended periods of time, nanoparticles have grown in importance as a subject of drug delivery research. Well-established protocols can be used to synthesize a wide variety of nanoparticles, such as quantum dots (Murray *et al.,* 1993), silica (Stober *et al.,* 1968), and noble metal nanoparticles (Schmid et al., 1992). Nanoparticles typically have a diameter of 1 to 100 nm in at least one dimension (Vert *et al.,* 2012). However, by enhancing bioavailability, solubility, and retention time, biodegradable nanoparticles are widely employed to increase the therapeutic efficacy of diverse water soluble/insoluble pharmaceuticals and bioactive compounds (Shenoy *et al.,* 2005). These medication formulations with nanoparticles lower toxicity risks and expenses for patients (Glen *et al.,* 2005**)**. An additional benefit of nanoparticles over bigger microparticles is their superior compatibility for intravenous (IV) distribution. The smallest capillaries possess a diameter of 5-7 mm. To prevent the particles from producing an embolism, the size of the particles being injected into the bloodstream must be much smaller than 5 mm, without aggregating.

Polymer nanoparticles are made from synthetic or natural polymers and have a diameter of less than 1 μm. Since natural polymers, such as proteins or polysaccharides, vary in purity and frequently need to be crosslinked, which may denature the comprised medication, they have not been employed extensively for this purpose. As a result, there has been a notable increase in the focus on synthetic polymers in this field. Poly (lactic acid) (PLA), Poly (glycolic acid) (PGA), and their copolymers, Poly(lactide-co-glycolide) (PLGA), have been the most commonly utilized polymers for nanoparticles. These polymers are recognized for their inherent ways of resorbability and biocompatibility. Polylactic acid and its copolymers with glycolic acid (PLGA) are commonly used in the production of sustained release preparations due to their biodegradability and biocompatibility (Anderson and Shive, 1997). Peptides and proteins, in particular, as well as traditional medicinal compounds, are being studied extensively for the controlled release of micro- and nanoparticles composed of PLGA copolymers. The routes of administration include nasal (Tobio *et al.,* 1998), pulmonary (O'Hara and Hickney, 2000), dermatological (De Galon et al., 2001), and ocular (Veloso et al., 1997; Moritera *et al.,* 1992). A number of techniques, including extrusion (Zhang *et al.,* 1994), spray drying (O'Hara and Hickney, 2000), and supercritical fluid extraction

(Kompella and Koushik, 2001), were proposed for the manufacture of PLGA microspheres. But the method that is most frequently employed is the emulsification solvent evaporation process (O'Donnell and McGinity, 1997). The PLGA polymer is dissolved in an organic solvent, then the PLGA solution is emulsified in a non-solvent (usually water) and the PLGA polymer precipitates as particles when the organic solvent evaporates. To stabilize the emulsion created during particle preparation, a stabilizer is typically added to the formulation. On the other hand, these stabilizers can also affect the characteristics of the particles that are created. The stabilizer type and concentration chosen may have an impact on the particle size. The stabilizer is present during particle formation at the boundary layer between the organic and water phases. It can also be incorporated on the surface of the particles to change their size, zeta potential, and mucoadhesion (Scholes *et al.,* 1999; Feng and Huang, 2001). Pluronic F68 is the most widely used stabilizer for PLGA nanoparticle synthesis in the literature. The objective was to investigate the effects of varying stabilizer concentrations on particle size during the nanoparticle manufacturing process. Finding the particle mean diameter, size distribution, and polydispersity are all part of the particle size analysis process. Photon correlation spectroscopy (PCS) or quasi-elastic light scattering (QELS) is a commonly used technique for size determination (Banerjee *et al.,* 2002**).** QELS measures the hydrodynamic diameter of the nanoparticles. According to a recent study, a greater knowledge of particle size and shape was obtained when PCS measurements were complemented by AFM measurements (Kumar *et al.,* 2004).

2. MATERIALS AND METHODS

PLGA copolymer (50/50, Mw 24-38 kDa) were purchased from Nomisma Health Care Private Limited. Pluronic F68 was supplied by HiMedia. Ethyl acetate (HPLC grade) was purchased from Merck. Water was purified by reverse osmosis (Milli-Q, Millipore).

2.1.Preparation of PLGA nanoparticles:

Nanoparticles were prepared by a typical solvent evaporation method (Vauthier *et al.,* 2009). PLGA polymer (0.05 g) dissolved in 5mL ethyl acetate was emulsified with the primary aqueous phase consists of 10 mL (0.2%) Pluronic F-68 in distilled water. The emulsion was sonicated for 1 min (in pulsed manner, 40% intensity) using a probe sonicator (SONICS & MATERIALS, Inc) over an ice bath and poured immediately into 100 mL aqueous solution of 0.2% Pluronic F-68 under magnetic stirring. The reaction was left to continue until the solvent evaporated and a

Fig. 1, 2, 3 DLS images of PLGA nanoparticles with 1.5 %,0.5%,0. 2% pluronic F 68 respectively

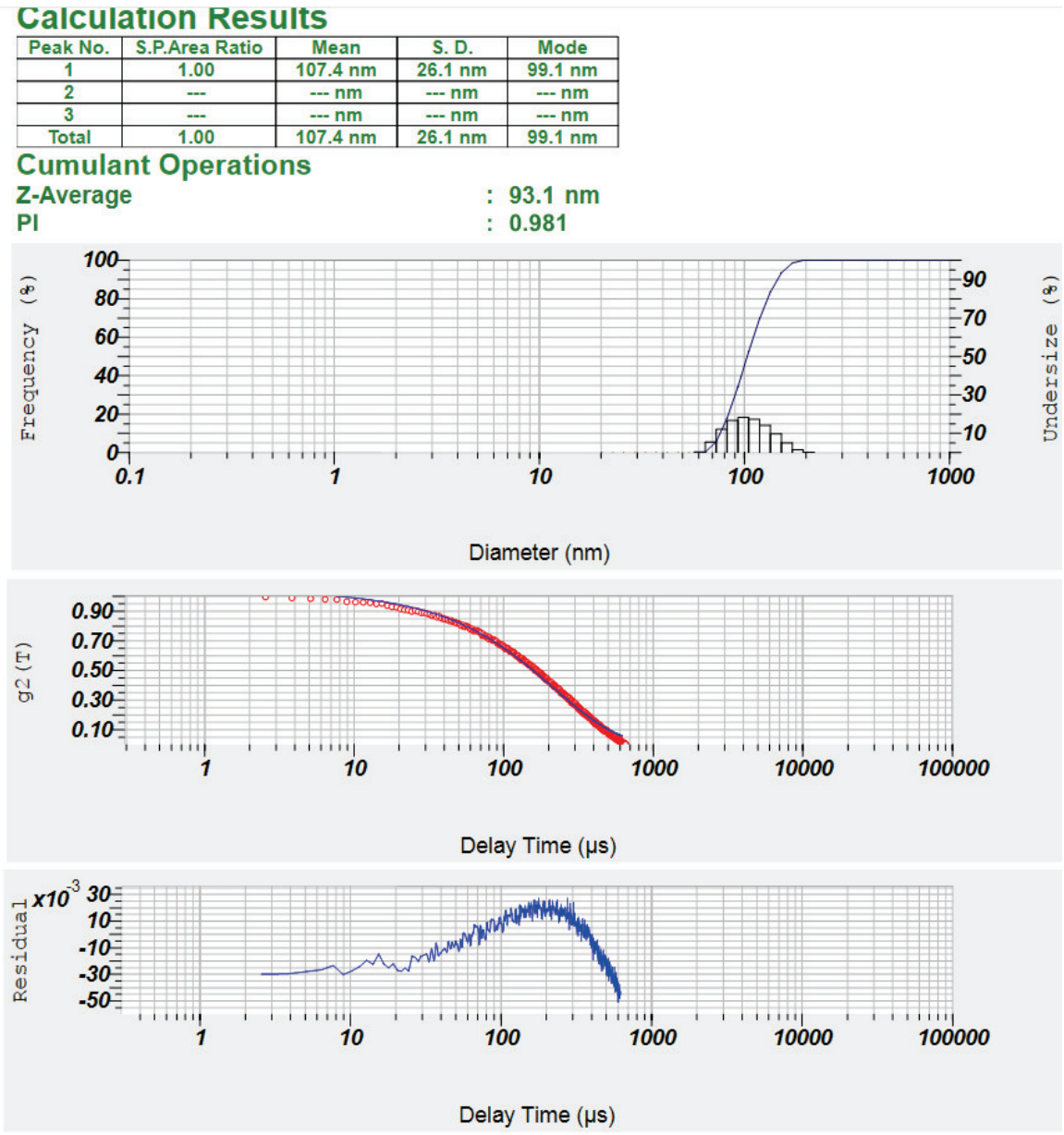
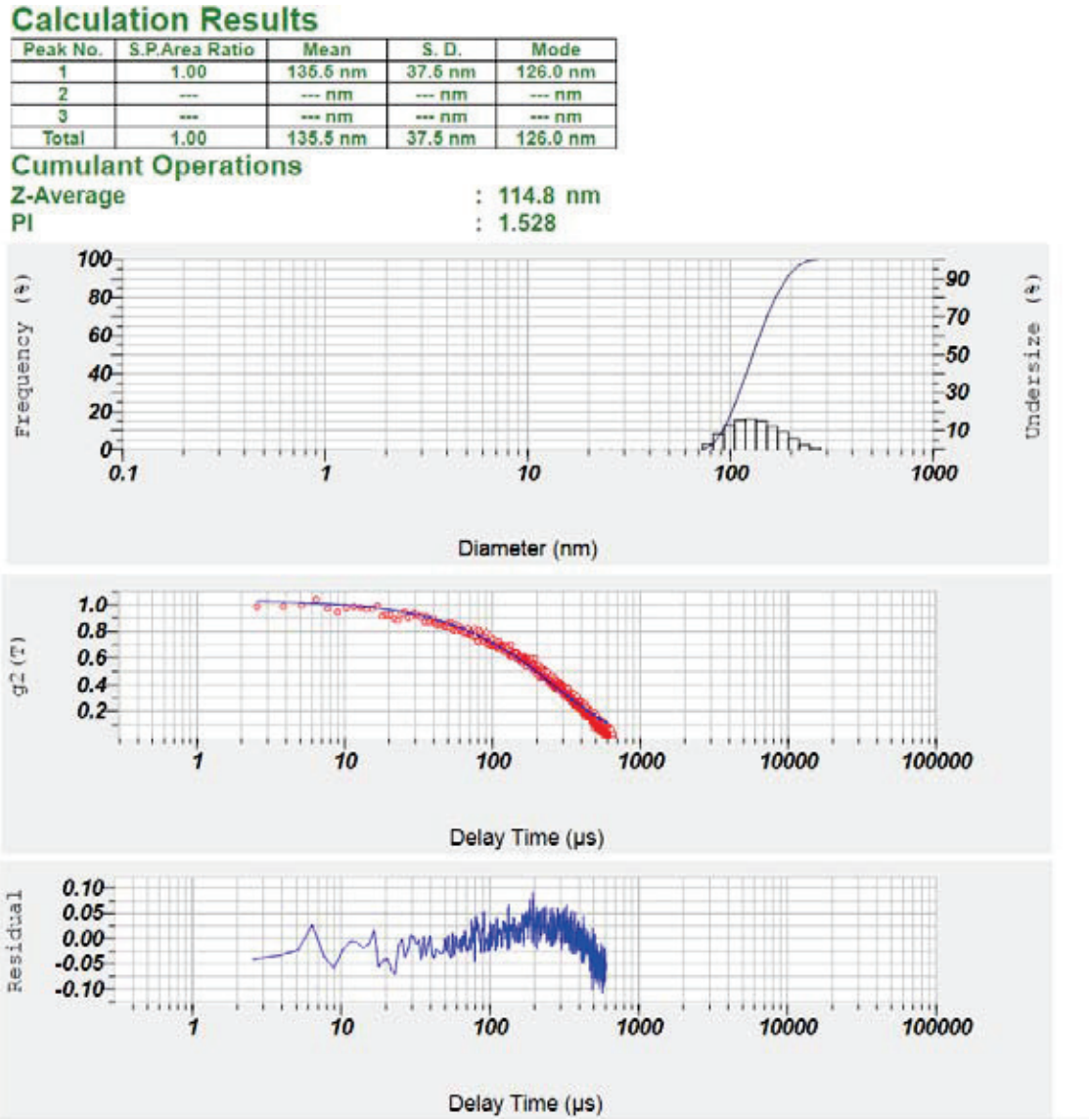


Table.1. Optimization of surfactant concentration with regard to average particle size

Formulation	Concentration of Pluronic F68 (% w/v)	Average particle size (nm)	Polydispersity index
PLGA NP	1.5	103.8	0.432
PLGA NP	0.5	107.4	0.981
PLGA NP	0.2	135.5	1.528

Fig. 2

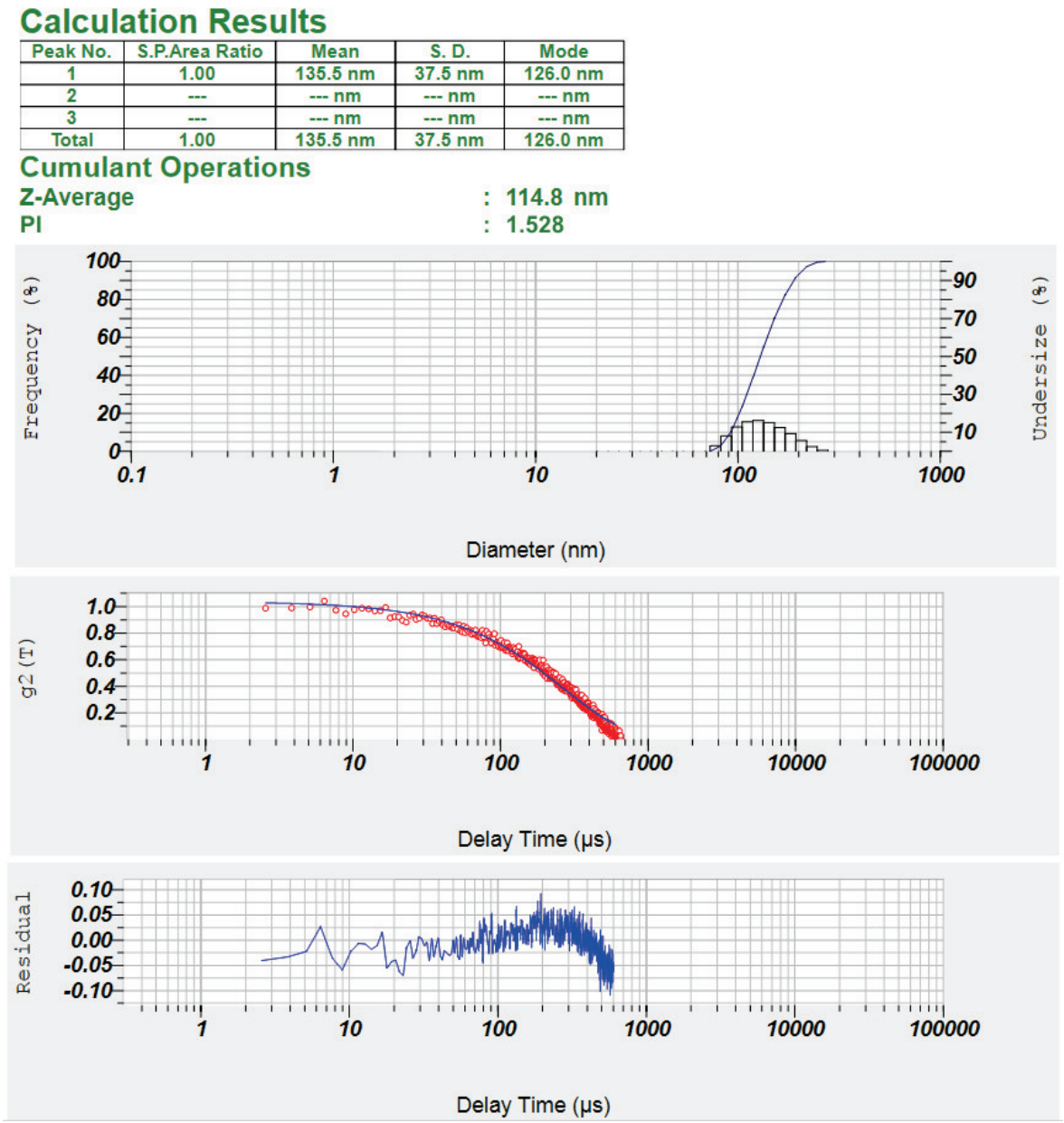


colloidal suspension of nanoparticles was obtained by centrifugation at 4000 rpm for 15 min.

2.2.Optimizationofsurfactantconcentration with regard to average particle size

In order to optimize the concentration of aqueous Pluronic F68 solution, the nanoparticles were prepared by using Pluronic F68 concentration of 0.2 to 1.5% and other parameters were kept constant. The Average particle size was determined using Laser Particle Size Analyzer (Horiba Scientific nanoPartica SZ-100V2 Series**).**

Fig. 3



3. RESULTS AND DISCUSSION

Single- or double-emulsion is a typical technique for creating PLGA particles, that enables for modification of particle parameters such size, encapsulant, and surface qualities (Jain *et al.,* 2000). Numerous factors affect these and other features, such as the type of solvent used, feed ratios, emulsification technique, and emulsifier type. But according to our observations, one experimenter can create particles with reliable characteristics.

The experimental parameter and the composition of the micro emulsion system, specifically the surfactant and co-surfactant employed, have an impact on the size of the nanoparticles. Reducing the concentration of surfactant resulted in an increase in particle size. With an increase in Pluronic F68 content, it was discovered that the mean nanoparticle size decreased. As the concentration of Pluronic F68 increased, so did the polydispersity index. The conclusion is that when Pluronic F68 concentration rises, more Pluronic F68 molecules overlap the surface of the droplet, protecting them from coalescence and producing smaller emulsion droplets.

4. SUMMARY

To summarize, there has been a notable effect on the size of PLGA nanoparticles when the surfactant content was optimized from 0.2% to 1.5%. It has been determined by careful evaluation and testing that a decrease in particle size is caused by an increase in surfactant concentration. The significance of the finding for the diverse uses of PLGA nanoparticles cannot be exaggerated, especially in drug delivery systems where the size of the particles greatly influences the effectiveness and biodistribution of the drug. Furthermore, this optimization approach not only improves the performance of PLGA nanoparticles but also provides information on the fundamental processes that control their synthesis and characteristics. Additional avenues for the advancement of nanoparticle-based technologies in other biological disciplines are expected to be revealed by further investigation into the optimization of surfactant concentration within this range.

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